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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/484,331	01/18/2000	John J. Harrington	5817-7L	9576
959	7590	12/23/2003	EXAMINER	
LAHIVE & COCKFIELD, LLP. 28 STATE STREET BOSTON, MA 02109			SHUKLA, RAM R	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

*S.M.*

## Office Action Summary

	Application No.	Applicant(s)	S.M.
	09/484,331	HARRINGTON ET AL.	
	Examiner	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

1) Responsive to communication(s) filed on 10 July 2003.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

4) Claim(s) 62 and 68-70 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 62, 68-70 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 18 January 2000 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) The translation of the foreign language provisional application has been received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_ .

2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ . 6) Other: \_\_\_\_\_ .

## **DETAILED ACTION**

1. The final rejection of 1-31-2003 has been withdrawn in view of a telephonic interview between Applicants' representative Anne Brown and Biotechnology Practice Specialist Brian Stanton on November 19, 2003, followed by Brian Stanton's discussion with SPE Deborah Reynolds and Examiner Shukla.
2. Rejections set forth in this office action are the only rejections pending in the instant application. Any rejection not repeated in this office action has been withdrawn.
3. Applicants' response and amendments filed 7-10-2003 have been entered.
4. Claims 62 and 68-70 are pending.
5. Persuant to the interview of 11/19/03, the following is the office action summary of the outstanding issues affecting patentability in the instant application:
  - Claims 62 and 68-70 contain new matter for reasons set forth below;
  - Claims 62 and 68-70 are not supported by an enabling disclosure because step (e) lacks enablement.

The issues are discussed in detail below.

### ***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
7. Claims 62 and 68-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claimed invention is a method of drug discovery comprising five steps: integrating a vector comprising a transcriptional regulatory sequence into the

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genome of eukaryotic cells wherein the integration of the vector activates the expression of an endogenous gene by means of said transcriptional regulatory sequence; culturing the cells; screening the cells for a cell in which a desired gene is activated or a phenotype is induced; treating said cell with one or more compounds and determining the ability of said one or more compound to interact with a product of said desired activated gene.

It is noted that the instant application is a divisional of the non-provisional application 09/276,820 and drug discovery claims with steps were first time presented at the filing of the instant application (1-18-00). The specification of the parent application 09/276,820 does not provide written support for a drug discovery claim with defined steps. The only references to the term drug discovery are: on page 7, lines 28-30, which only states:

"The expression product can then be isolated and purified to use, for example, in protein therapy or drug discovery";

or on page 11, lines 27-29 continued on page 12, lines 1 and 2, which states:

"In highly preferred embodiments, the cells expressing the endogenous gene product are cultured under conditions favoring production of sufficient amounts of gene product for commercial application, and especially for diagnostic, therapeutic and drug discovery uses".

None of these sections or any other section of the specification as filed on 1-18-00 teaches a drug discovery method. It is noted that claims 62 and 68-70 recites specific steps (a)-(e), however, there is no written support for these steps in the instant application or in the parent application.

Therefore, instantly pending claims 62 and 68-70 are considered new matter.

8. Claim 62 and 68-70 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

Claimed invention is a method of drug discovery comprising five steps: integrating a vector comprising a transcriptional regulatory sequence into the genome of eukaryotic cells wherein the integration of the vector activates the expression of an endogenous gene by means of said transcriptional regulatory sequence; culturing the cells; screening the cells for a cell in which a desired gene is activated or a phenotype is induced; treating said cell with one or more compounds and determining the ability of said one or more compound to interact with a product of said desired activated gene.

The specification as filed does not provide any guidance for practicing a method of drug discovery and an artisan of skill would have required extensive experimentation to practice the claimed method and such experimentation would

have been considered undue because the experimentation would not have been routine at the time of the invention as discussed below.

First, the specification does not teach any method of drug discovery, either using cells or protein product purified from cells. As noted in the previous paragraph (paragraph #5), the only references to a term “drug discovery” are on pages 7 and 11, however, these sections of the specification do not teach how to practice the claimed drug discovery methods. The step (a) of the claimed method encompasses activation of an endogenous gene by integrating a vector comprising a transcriptional regulatory sequence into the gene by any mechanism, including homologous recombination. However, the specification does not teach such a method, rather it teaches activation of endogenous genes by non-targeted integration of specialized activation vectors (see lines 2-11 on page 1 of the specification). Therefore, the specification teaches away from integrating the vector by homologous recombination. In other words the specification only teaches a method of non-targeted activation.

As discussed previously, the specification did not teach any method of drug discovery. An artisan would have depended on the teachings in the art at the time of the invention to practice the claimed method of drug discovery. While it would have been routine to culture a cell, expose it to compound (steps b-d of the claimed method), it would not have been routine to determine the ability of one or more compounds to interact with the product of the activated gene since such would have depended on the characteristics/properties of the gene or gene product and the compound. This in turn would require characterization of the gene or gene product and a compound, which could interact with the gene product. Additionally, for determining the interaction of a compound with a gene product, an artisan would need to know the structure of the compound, structure of the gene product and requirements for the interaction of the compound to interact with a gene product. The specification does not provide any guidance as to how to determine the ability of one or more compounds to interact with a product of an activated gene, what characteristics of a gene product or compound will be used in determining such. The specification does not provide any guidance as to how to

determine these parameters. In the absence of any teaching in the specification, an artisan of skill would not have been able to determine whether the product of the activated gene interacts with a test compound when the activated gene is random, unknown and uncharacterized. Further one would not know what parameters to use for determining the interaction of any compound with any product of a gene; and how to determine such an interaction.

Additionally, it is emphasized that even when a cell in which a desired gene is activated, there is no way of knowing if the desired phenotype observed in a selected cell is due to the activated expression of only the desired gene or due to a activation of multiple genes. In fact, the specification on page 32, lines 28-30, states that a single cell or different cells in a set of transfectants (library) can over express more than one protein following transfection with the same or different constructs. The specification does not teach as to how an artisan would have determined that a compound, in step e, interacted with the gene product of the desired gene, not with the product of any other gene.

In summary, the specification, except for a mere germ idea of drug discovery, does not teach how to practice a method of drug discovery. While a general method of drug screening might have been routine in the art by adding a compound(s) to cells in culture and screen for a phenotype, neither the specification nor the art teaches how to determine the interaction of one or more compounds with a product of a gene and therefore, an artisan would not have any guidance from the specification or in the prior art for practicing the claimed invention and would require extensive experimentation for practicing the claimed method. It is noted that such experiments would not have been routine at the time of the invention and therefore, an artisan would have required undue experimentation to practice the claimed invention.

### ***Response to Arguments***

Applicant's arguments with respect to claims 62 and 68-70 have been considered but are moot in view of the new ground(s) of rejection.

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9. Applicant's attention is drawn directed to step (e), particularly, if step (e) were to be deleted, the claims would be subject to one or more prior art rejections.

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

Please note that effective January 13, the offices for Examiner Shukla, SPE Reynolds and LIE William Phillips will move to the new USPTO location in Alexandria, VA and their phone numbers will change. The new phone numbers will be as follows:

Ram Shukla: **(571) 272-0735**

Deborah Reynolds: **(571) 272-0734**

William Phillips: **(571) 272-0548**

Ram R. Shukla, Ph.D.  
Primary Examiner  
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